#### Figure 1

MAMSSGGSGGGVPEQEDSVLFRRGTGQSDDSDIWDDTALIKAYDKAVASFKHALKNG DICETSGKPKTTPKRKPAKKNKSQKKNTAASLQQWKVGDKCSAIWSEDGCIYPATIA SIDFKRETCVVVYTGYGNREEQNLSDLLSPICEVANNIEQNAQENENESQVSTDESE NSRSPGNKSDNIKPKSAPWNSFLPPPPPMPGPRLGPGKPGLKFNGPPPPPPPPPHL LSCWLPPFPSGPPIIPPPPPICPDSLDDADALGSMLISWYMSGYHTGYYMGFRQNQK EGRCSHSLN



#### Figure 2A



CGGGGCCCCACGCTGCGCACCCGCGGGTTTGCTATGGCGATGAGCAGCGGCGGCAGT GGTGGCGCGCCCGGAGCAGGAGGATTCCGTGCTGTTCCGGCGCGCACAGGCCAG AGCGATGATTCTGACATTTGGGATGATACAGCACTGATAAAAGCATATGATAAAGCT GTGGCTTCATTTAAGCATGCTCTAAAGAATGGTGACATTTGTGAAACTTCGGGTAAA CCAAAAACCACACCTAAAAGAAAACCTGCTAAGAAGAATAAAAGCCAAAAGAAGAAT ACTGCAGCTTCCTTACAACAGTGGAAAGTTGGGGACAAATGTTCTGCCATTTGGTCA GAAGACGGTTGCATTTACCCAGCTACCATTGCTTCAATTGATTTTAAGAGAGAAACC TGTGTTGTGGTTTACACTGGATATGGAAATAGAGAGGAGCAAAATCTGTCCGATCTA CTTTCCCCAATCTGTGAAGTAGCTAATAATATAGAACAGAATGCTCAAGAGAATGAA AATGAAAGCCAAGTTTCAACAGATGAAAGTGAGAACTCCAGGTCTCCTGGAAATAAA CCCATGCCAGGGCCAAGACTGGGACCAGGAAAGCCAGGTCTAAAATTCAATGGCCCA CCTTCTGGACCACCAATAATTCCCCCACCACCTCCCATATGTCCAGATTCTCTTGAT GATGCTGATGCTTTGGGAAGTATGTTAATTTCATGGTACATGAGTGGCTATCATACT AATTAAGGAGAAATGCTGGCATAGAGCAGCACTAAATGACACCACTAAAGAAACGAT CAGACAGATCTGGAATGTGAAGCGTTATAGAAGATAACTGGCCTCATTTCTTCAAAA TATCAAGTGTTGGGAAAGAAAAAGGAAGTGGAATGGGTAACTCTTCTTGATTAAAA GTTATGTAATAACCAAATGCAATGTGAAATATTTTACTGGACTCTTTTGAAAAACCA TCTGTAAAAGACTGAGGTGGGGGGGGGGGGCCAGCCACGGTGGTGAGGCAGTTGAGAA CCTGTGAGAAGGGTGTTGTAGTTTATAAAAGACTGTCTTAATTTGCATACTTAAGCA TTTAGGAATGAAGTGTTAGAGTGTCTTAAAATGTTTCAAATGGTTTAACAAAATGTA TGTGAGGCGTATGTGGCAAAATGTTACAGAATCTAACTGGTGGACATGGCTGTTCAT TGTACTGTTTTTTTCTATCTTCTATATGTTTAAAAGTATATAAAAAATATTTAAT 

#### Figure 2B



AATTTTTAAATTTTTTGTAGAGACAGGGTCTCATTATGTTGCCCCAGGGTGGTCAA GCTCCAGGTCTCAAGTGATCCCCCTACCTCCGCCTCCCAAAGTTGTGGGATTGTAGG CATGAGCCACTGCAAGAAAACCTTAACTGCAGCCTAATAATTGTTTTCTTTGGGATA ACTTTTAAAGTACATTAAAAGACTATCAACTTAATTTCTGATCATATTTTGTTGAAT AAAATAAGTAAAATGTCTTGTGAACAAAATGCTTTTTAACATCCATATAAAGCTATC TATATATAGCTATCTATATCTATATAGCTATTTTTTTTAACTTCCTTTTATTTTCCT TACAG\*GGTTTTAGACAAAATCAAAAAGAAGGAAGGTGCTCACATTCCTTAAATTAA GGA\*GTAAGTCTGCCAGCATTATGAAAGTGAATCTTACTTTTGTAAAACTTTATGGT TTGTGGAAAACAAATGTTTTTGAACAGTTAAAAAGTTCAGATGTTAGAAAGTTGAAA GGTTAATGTAAAACAATCAATATTAAAGAATTTTGATGCCAAAACTATTAGATAAAA AACATACTTTCACAATAAAGAGCTTTAGGATATGATGCCATTTTATATCACTAGTAG GCAGACCAGCAGACTTTTTTTTTTTTGTGATATGGGATAACCTAGGCATACTGCACTG TACACTCTGACATATGAAGTGCTCTAGTCAAGTTTAACTGGTGTCCACAGAGGACAT GGTTTAACTGGAATTCGTCAAGCCTCTGGTTCTAATTTCTCATTTGCAG\*GAAATGC GTGAAGCGTTATAGAAGATAACTGGCCTCATTTCTTCAAAATATCAAGTGTTGGGAA AGAAAAAAGGAAGTGGAATGGGTAACTCTTCTTGATTAAAAGTTATGTAATAACCAA ATGCAATGTGAAATATTTTACTGGACTCTTTTGAAAAACCATCTGTAAAAGACTGAG GTGGGGGTGGAGGCCAGCACGGTGGTGAGGCAGTTGAGAAAATTTGAATGTGGATT AGATTTTGAATGATATTGGATAATTATTGGTAATTTTATGGCCTGTGAGAAGGGTGT TGTAGTTTATAAAAGACTGTCTTAATTTGCATACTTAAGCATTTAGGAATGAAGTGT CAAAATGTTACAGAATCTAACTGGTGGACATGGCTGTTCATTGTACTGTTTTTTCT ATCTTCTATATGTTTAAAAGTATATAATAAAAATATTTAATTT



#### Figure 3A

1

2

\*AGCGATGATTCTGACATTTGGGATGATACAGCACTGATAAAAGCATATGATAAAGC
TGTGGCTTCATTTAAGCATGCTCTAAAGAATGGTGACATTTGTGAAACTTCGGGTAA
ACCAAAAACCACACCTAAAAGAAAACCTGCTAAGAAGAATAAAAGCCAAAAGAAGAA

3

TACTGCAGCTTCCTTACAACAG\*TGGAAAGTTGGGGACAAATGTTCTGCCATTTGGT CAGAAGACGGTTGCATTTACCCAGCTACCATTGCTTCAATTGATTTTAAGAGAGAAA CCTGTGTTGTGGTTTACACTGGATATGGAAATAGAGAGGAGCAAAATCTGTCCGATC

1

5

6

ATTTCCTTCTGGACCACCA\*ATAATTCCCCCACCACCTCCCATATGTCCAGATTCTC
TTGATGATGCTGATGCTTTGGGAAGTATGTTAATTTCATGGTACATGAGTGGCTATC

ATACTGGCTATTATATG\*GGTTTCAGACAAAATCAAAAAGAAGGAAGGTGCTCACAT



#### Figure 3B

AATTTTTAAATTTTTTGTAGAGACAGGGTCTCATTATGTTGCCCCAGGGTGGTCTCAA GCTCCAGGTCTCAAGTGATCCCCCTACCTCCGCCTCCCAAAGTTGTGGGATTGTAGG CATGAGCCACTGCAAGAAACCTTAACTGCAGCCTAATAATTGTTTTCTTTGGGATA ACTTTTAAAGTACATTAAAAGACTATCAACTTAATTTCTGATCATATTTTGTTGAAT AAAATAAGTAAAATGTCTTGTGAACAAAATGCTTTTTAACATCCATATAAAGCTATC TATATATAGCTATCTATGTCTATATAGCTATTTTTTTTTAACTTCCTTTTATTTTCCT TACAG\*GGTTTCAGACAAAATCAAAAAGAAGGAAGGTGCTCACATTCCTTAAATTAA GGA\*GTAAGTCTGCCAGCATTATGAAAGTGAATCTTACTTTTGTAAAACTTTATGGT TTGTGGAAAACAAATGTTTTTGAACAGTTAAAAAGTTCAGATGTTAAAAAAGTTGAAA GGTTAATGTAAAACAATCAATATTAAAGAATTTTGATGCCAAAACTATTAGATAAAA AACATACTTTCACAATAAAGAGCTTTAGGATATGATGCCATTTTATATCACTAGTAG GCAGACCAGCAGACTTTTTTTTTTTTTTTTTGTGATATGGGATAACCTAGGCATACTGCACTG TACACTCTGACATATGAAGTGCTCTAGTCAAGTTTAACTGGTGTCCACAGAGGACAT GGTTTAACTGGAATTCGTCAAGCCTCTGGTTCTAATTTCTCATTTGCAG\*GAAATGC GTGAAGCGTTATAGAAGATAACTGGCCTCATTTCTTCAAAATATCAAGTGTTGGGAA AGAAAAAAGGAAGTGGAATGGGTAACTCTTCTTGATTAAAAGTTATGTAATAACCAA ATGCAATGTGAAATATTTTACTGGACTCTTTTGAAAAACCATCTGTAAAAAGACTGGG GTGGGGGTGGGAGGCCAGCACGGTGGTGAGGCAGTTGAGAAAATTTGAATGTGGATT AGATTTTGAATGATATTGGATAATTATTGGTAATTTTATGGCCTGTGAGAAGGGTGT TGTAGTTTATAAAAGACTGTCTTAATTTGCATACTTAAGCATTTAGGAATGAAGTGT CAAAATGTTACAGAATCTAACTGGTGGACATGGCTGTTCATTGTACTGTTTTTTTCT ATCTTCTATATGTTTAAAAGTATATAATAAAAATATTTAATTT



#### Figure 4

#### C212

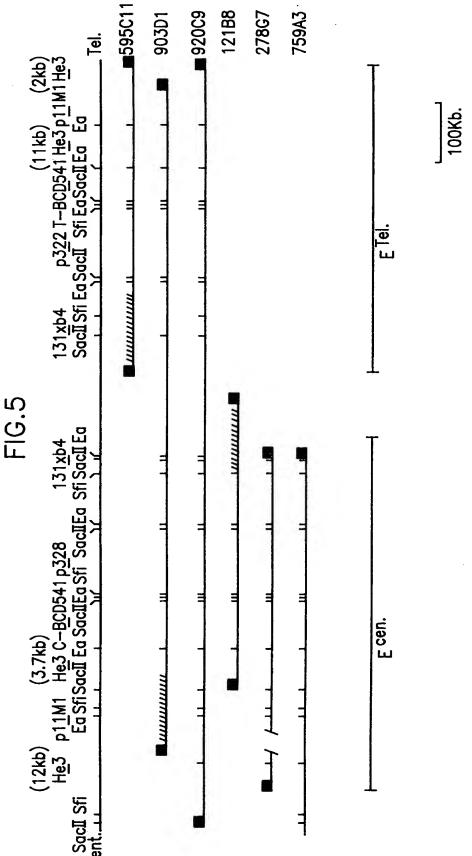
#### C272

#### AFM157xd10

#### C161

#### C171

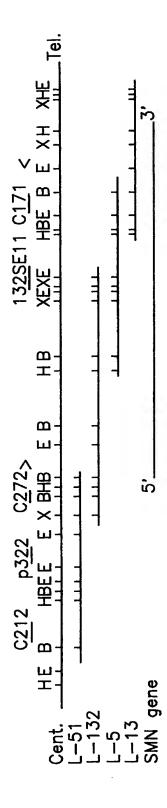




Restriction map of the 5q13 region for Eagl(Ea), SacII (SacII), SfiI (Sfi). Numbers under parenthesis indicate Centromer(Cent.), Telomere (Tel.). Probes are indicated above the restriction map. YACS are below the the restriction fragment detected by He3; Telomeric element (ETel ),centromeric element (Ecen), restriction map.



FIG. 6



map shows polymorphic markers C21 containing the survival motor-neuron direction of ð The position are also and Tel. XbaI(X) C272 and C171. Physical map shows location and SMA patients transcription of SMN gene; phage clones used physical map. Restriction map for EcoRI(E), respectively. SacII(S) are shown. Cent genomic rearrangements found in indicate centromere and telomere Telomeric element (SMN gene). Hind目(H), ndicated. gene



GENE DOSAGE ANALYSIS OF THE 5q13 REGION WITH THE 132SE11 PLASMID CONE IN SMA TYPE I PATIENT. TOTAL HUMAN DNA FROM SMA FAMILY WAS DIGESTED WITH HINDIII FOR SOUTHERN BLOTTING. FILTER WAS CONSECUTIVELY HYBRIDIZED WITH 132SE11 (A) AND JK53 PROBES (B). A SIGNIFICANT DECREASE IN 132SE11 BAND INTENSITY, WHICH INDICATED THE DELETION, COMPARED WITH THEIR PARENTS. F/FATHER, M/MOTHER, A /AFFECTED



FIG. 7

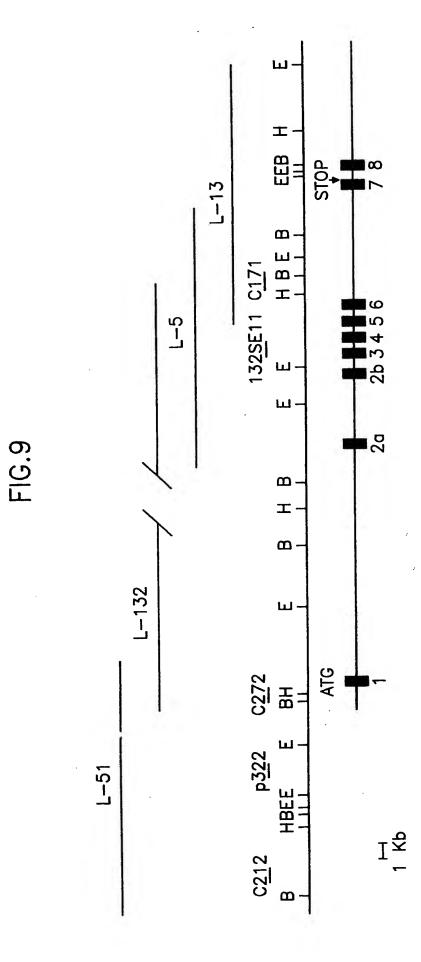
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#### REPLACEMENT SHEET

#### Figure 8

MAMSSGGSGGGVPEQEDSVLFRRGTGQSDDSDIWDDTALIKAYDKAVASFKHALKNG DICETSGKPKTTPKRKPAKKNKSQKKNTAASLQQWKVGDKCSAIWSEDGCIYPATIA SIDFKRETCVVVYTGYGNREEQNLSDLLSPICEVANNIEQNAQENENESQVSTDESE NSRSPGNKSDNIKPKSAPWNSFLPPPPPMPGPRLGPGKPGLKFNGPPPPPPPPPHL LSCWLPPFPSGPPIIPPPPPICPDSLDDADALGSMLISWYMSGYHTGYYM





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#### REPLACEMENT SHEET

#### Figure 10A

cctcccgggcaccgtactgttccgctcccagaagccccggggcgccggaagtcgtcac tcttaagaagggacggggcccacgctgcgcacccgcgggtttgct ATG GCG Μ Α ATG AGC AGC GGC AGT GGT GGC GGC GTC CCG GAG CAG GAG G G S G G G V P GAT TCC GTG CTG TTC CGG CGC GGC ACA GGC CAG gtgaggtcgcagc D F R R G  $\mathbf{T}$ G 0 cagtgcagtctccctattagcgctctcagcacccttcttccggcccaactctccttc cqca 2a attaaacctatctgnacatgagttgtttttatttcttaccctttccag AGC GAT D GAT TCT GAC ATT TGG GAT GAT ACA GCA CTG ATA AAA GCA TAT D S Ι W D D D  $\mathbf{T}$ Α  $\mathbf{L}$ Ι GAT AAA GCT GTG GCT TCA TTT AAG gtatqaaatgcttgnttagtcgttt D K Α V Α S F K tcttattttctcgttattcatttggaaaggaattgataacatacgataaagtqttaa 2b aggtgctttctgaggtgacggagccttgagactagcttatagtagtaactgggttat gtcgtgacttttattctgtgcaccaccctgtaacatgtacatttttattcctatttt cqtaq CAT GCT CTA AAG AAT GGT GAC ATT TGT GAA ACT TCG GGT Η Α  $\mathbf{L}$ G K Ν D I C E  $\mathbf{T}$ G AAA CCA AAA ACC ACA CCT AAA AGA AAA CCT GCT AAG AAG AAT K Т K P K R K K Ρ K AAA AGC CAA AAG AAG AAT ACT GCA GCT TCC TTA CAA CAG gttat K K K N  $\mathbf{T}$ Α Α S  $\mathbf{L}$ Q tttaaaatgttgaggatttaacttcaaaggatgtctcattagtccttatttaatagt gtaaaatgtctttaact 3 gcctgcaggtcgatcaaaacgagatgatagtttgccctcttcaaaagaaatgtgtgc atgtatatatctttgatttcttttgtag TGG AAA GTT GGG GAC AAA TGT K G D K C TCT GCC ATT TGG TCA GAA GAC GGT TGC ATT TAC CCA GCT ACC S Ι S Ē D G C Ι Y P Α ATT GCT TCA ATT GAT TTT AAG AGA GAA ACC TGT GTT GTG GTT Ι Α S Ι D F K R Ε  $\mathbf{T}$ C V V V TAC ACT GGA TAT GGA AAT AGA GAG GAG CAA AAT CTG TCC GAT G Y G Ν R E Ε Q Ν  $\mathbf{L}$ S D CTA CTT TCC CCA ATC TGT GAA GTA GCT AAT AAT ATA GAA CAG  $\mathbf{L}$ L S Ρ Ι C E V Α Ν N Ι E Q



#### Figure 10B

AAT GCT CAA GAG gtaaggatacaaaaaaaaaaaaaaattcaatttctggaagcag Ν Α 0 agactagatgagaaactgttaaacagtatacaca ccaccgaggcattaattttttcttaatcacacccttataacaaaaacctgcatattt tttctttttaaag AAT GAA AAT GAA AGC CAA GTT TCA ACA GAT GAA Ε Ν Ε S  $Q \cdot V$ S D Ν AGT GAG AAC TCC AGG TCT CCT GGA AAT AAA TCA GAT AAC ATC S Ε Ν S R S Ρ G Ν  $\mathbf{K}$ S D Ν Ι AAG CCC AAA TCT GCT CCA TGG AAC TCT TTT CTC CCT CCA CCA Ρ Ρ P K S Α Ρ W Ν S F L CCC CCC ATG CCA GGG CCA AGA CTG GGA CCA GGA AAG gtaaacctt Ρ G Ρ  $\mathbf{L}$ G Ρ G K R ctatgaaagttttccagaaaatagttaatgtcgggacatttaacctctctgttaact aatttqtaqctctccca caaatattctqqqtaattatttttatccttttqqtttttqaqtcctttttattcctat catattgaaattggtaagttaattttcctttgaaatattccttatag CCA GGT G CTA AAA TTC AAT GGC CCA CCA CCG CCA CCG CCA CCA CCA Ρ L K F N G Ρ Ρ Ρ Ρ Ρ Ρ Ρ Ρ CCC CAC TTA CTA TCA TGC TGG CTG CCT CCA TTT CCT TCT GGA P Ρ H S C W Τ, F CCA CCA qtaaqtaaaaaqaqtataqqttaqattttqctttcacatacaatttqa Р Ρ taatta ccagacttta::tttttgtttactggatataaacaatatctttttctgtctccag. ATA ATT CCC CCA CCA CCT CCC ATA TGT CCA GAT TCT CTT GAT P Ι I Ρ Ρ Ρ Ρ Ρ Ι С D S  $\mathbf{L}$ D GAT GCT GAT GCT TTG GGA AGT ATG TTA ATT TCA TGG TAC ATG S Y Μ D Α Α L G S M L Ι W AGT GGC TAT CAT ACT GGC TAT TAT ATG gtaagtaatcactcagcatct S G Η Т G Y Υ Μ tttcctqacaatttttttqtaqttatqtqactttqtttqqtaaatttataaaatact acttq 7 aactgcagcctaataattgttttctttgggataacttttaaagtacattaaaagact

atcaacttaatttctgatcatattttgttgaataaaataagtaaaatgtcttgtgaa



#### Figure 10C

 $\rightarrow$  a

 $\rightarrow$  T

atagctattttttttaacttccttttattttccttacag GGT TTC AGA CAA

G F R Q

AAT CAA AAA GAA GGA AGG TGC TCA CAT TCC TTA AAT <a href="taaggag">taaggag</a>ta N O K E G R C S H S L N \*

aagtctgccagcattatgaaagtgaatcttacttttgtaaaactttatggtttgtgg

 $\rightarrow$   $\dot{c}$ 

aaaacaatgtttttgaacagttaaaaagttcagatgttaaaaagttgaaaggttaa tgtaaaacaatcaatattaaagaattttgatgccaaaactattagataaaaggttaa

 $\rightarrow$  g

8

 $\rightarrow$  a

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#### REPLACEMENT SHEET

### Figure 11

gatctgcc	cttcc	cttcc	etge	ccca	atgtt	tgto	CTTTC	cctt	gttt	gtcttta	50
tatagato	caago	caggt	ttta	aaatt	ccta	agtag	ggago	cttad	catt	cactttt	100
ccaagggg	ggagg <b>F-1</b>	iāāā	aataa <b>GH</b>	aatat	cta	cacao	cacao	cacao	cacao	<b>cacac</b> ca	150
cactggag		gagad		gccta		aacat FF-1	gcc	gaaa	cccc	gtctcta	200
ctaaatad	caaaa	aaata	agct	gagct			gcac	gccta	atagi	cctagc	250
tactgggg			ggtg	ggag	gatc	gctt	gagco	ccaa	gaagt	cgaggc	300
tgcagtga	space.		cgc	gccg	ctgca	actco	cage	ctga	gcga	cagggcg	350
aggctctg	gtcto	caaaa	acaaa	acaaa	acaaa	aaaa				<u>a</u> aatata	400
acacagto	gaaat	cgaaa	aggat	tga	gagaa <b>HiN</b> I		_	3- <b>IF</b> atata		gccacaa	450
atgtggga	agggo	cgata	aacca	actc			cgtga	agaa	gtta	ctacaag	500
cggtcct	cccg	ggca	ccgta	actg	ttcc	gctco	ccaga	aag <u>c</u>	cccg		550
gaagtcgt		cctta	aagaa	aggga	acgg	ggcc	ccac	gctg			600
<b>E41</b> gtttgct		GCG	ATG	AGC	AGC	GGC	GGC	AGT	GGT	GGC	637
55-0	М	A	М	S		G	G	S	G	G	



### Figure 12A

cggcgtggtagcaggcc							AGT Ser		41	
								TTC Phe		80
								TGG Trp		119
								GTG Val		158
								TGT Cys		197
								AAA Lys		236
								ACA Thr		275
								TCT Ser		314
								ACT Thr		353
								GTG Val		392
								TTA Leu		431
								AGT Ser		470
								TCC Ser		509
								AGT Ser		548

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#### REPLACEMENT SHEET

### Figure 12B

		GCT Ala					587
		CCA Pro					626
		TTC Phe					665
		CCC Pro					704
		CCA Pro					743
		TGT Cys					782
 	 	 TCT Ser					821
 		GGT Gly					860
		ACA Thr	taaq *	<b>J</b>			885

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#### REPLACEMENT SHEET

### Figure 13

20 GSGGGVPEQE ====	30 DSVLFRRGTG =-=====				
GSGGAGSEQE 2	DTVLFRRGTG	QSDDSDIWD			
80 GKPKTTPKRK ===-= -==		NTAASLQQW	110 KVGDKCSAIW	SEDGCIYPA'	
DKPKGTARRK 70	PAKKNKSQKK	NATTPLKQW 90	KVGDKCSAVW 100	SEDGCIYPA' 110	TITSIDFKR 120
140 ETCVVVYTGY			NNIEQNAQEN		- ESENSRSPG
ETCVVVYTGY 130	GNREEQNLSD 140	LLSPTCEVA	NSTEQNTQEN 160	IE—-SQVSTDI 170	
90 2 NKSDNIKPKS	APWNSFLPPP			230 [PPPPPPPPP]	240 PHLLSCWLP
RSKAHSKSKA 80 1	APWTSFLPPP	PPMPGSGLG	PGKPGLKFNG 210	PPPPPPLPPI 220	PPFLPCWMP 230
250 PFPSGPPIIP		270 DDADALGSM	280 LISWYMSGYH	,	300 NQKEGRCSH
PFPSGPPIIP 240	PPPPISPDCL 250	DDTDALGSM 260	LISWYMSGYH 270	TGYYMGFRQI 280	NKKEGKCSH 290

ŞL

TN



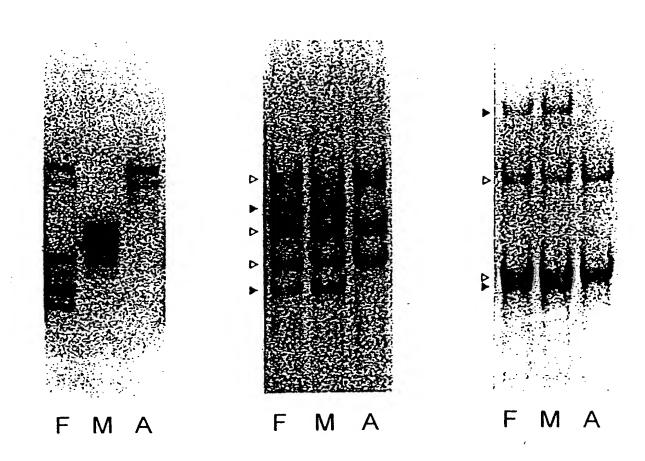


FIG. 14(A) FIG. 14(B) FIG. 14(C)



### SSCP ANALYSIS







121B8 YAC
595CII YAC
HUMAN 1 CONTROL
HUMAN 2 CONTROL
HUMAN 3 CONTROL
HUMAN 4 SMA

FIG. 15

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